

# **EXHIBIT 22**

# Asbestos-Related Pleural Diseases: Dimensional Criteria Are Not Appropriate to Differentiate Diffuse Pleural Thickening From Pleural Plaques

Jacques Ameille, MD,<sup>1,2\*</sup> Mireille Matrat, MD,<sup>2,3</sup> Christophe Paris, MD,<sup>4</sup>  
Nathalie Joly, MD,<sup>1,2</sup> Claude Raffaelli, MD,<sup>5</sup> Patrick Brochard, MD,<sup>6</sup>  
Yuriko Iwatsubo, MD,<sup>7</sup> Jean Claude Pairon, MD,<sup>2,3</sup> and Marc Letourneux, MD<sup>5</sup>

**Background** In the literature, the criteria used to define pleural plaques (PP) and diffuse pleural thickening (DPT) are very heterogeneous and often imprecise. A multicenter retrospective study was conducted to assess the relevance of two radiographic definitions of DPT. **Methods** The study population consisted of 287 subjects with asbestos-related pleural thickening. Two definitions were used to characterize DPT on postero-anterior chest radiographs: definition 1: pleural thickening associated with obliteration of the costophrenic angle; definition 2: pleural thickening at least 5 mm wide, extending for more than one quarter of the chest wall. Prevalence of respiratory symptoms and pulmonary function tests were compared in the DPT and PP groups resulting from the two definitions of DPT. **Results** According to definition 1, 34 patients (11.8%) were classified in the DPT group. Prevalence of chronic sputum, dyspnea, and chest pain was significantly higher in this group than in the PP group. FEV<sub>1</sub>, FVC, and TLC were significantly lower. The differences persisted after adjustment for confounding factors. According to definition 2, 102 patients (36.6%) were classified in the DPT group. DPT and PP groups did not differ in terms of prevalence of respiratory symptoms, or pulmonary function tests. Agreement between readers was significantly better when using definition 1.

**Conclusions** Obliteration of costophrenic angle is a much more reliable sign than dimensional criteria to characterize DPT. *Am. J. Ind. Med.* 45:289–296, 2004.

© 2004 Wiley-Liss, Inc.

**KEY WORDS:** asbestos; diffuse pleural thickening; pleural plaques; ILO classification

<sup>1</sup>Unité de Pathologie Professionnelle et de Santé au Travail, Hôpital Raymond Poincaré AP-HP, Garches, France

<sup>2</sup>Institut Interuniversitaire de Médecine du Travail de Paris Ile-de-France, Paris, France

<sup>3</sup>Service de Pneumologie et de Pathologie Professionnelle, Créteil, France

<sup>4</sup>Service de Pathologie Professionnelle, Rouen, France

<sup>5</sup>Service de Pathologie Professionnelle, Caen, France

<sup>6</sup>Service de Pathologie Professionnelle, Bordeaux, France

<sup>7</sup>INSERM EMI 03 37 Créteil, France

Contract grant sponsor: Caisse Régionale d'Assurance Maladie d'Ile-de-France (Paris, France).

\*Correspondence to: Prof. Jacques Ameille, Unité de Pathologie Professionnelle et de Santé au Travail, Hôpital Raymond Poincaré, 104 Boulevard Raymond Poincaré, 92380 GARCHES. E-mail: jacques.ameille@rpc.ap-hop-paris.fr

Accepted 28 October 2003

DOI 10.1002/ajim.10341. Published online in Wiley InterScience (www.interscience.wiley.com)

## INTRODUCTION

Pleural fibrosis is by far the most frequent non-malignant asbestos-related disease. The distinction between pleural plaques (PP)—fibrosis of the parietal pleura—and diffuse pleural thickening (DPT), which is usually considered to result from thickening and fibrosis of the visceral pleura with fusion of the parietal pleura, is important because PP are generally considered to be indicators of asbestos exposure with a modest effect on lung function, whereas DPT might be associated with significant functional impairment [Schwartz, 1991; Rudd, 1996; Ameille and Letourneux, 1998; Chailleux and Letourneux, 1999]. Moreover, DPT

occurs with higher fiber burdens than PP [Gibbs et al., 1991] so that subjects with asbestos-induced DPT, might be at higher risk of developing other asbestos-related diseases, particularly lung cancer, than those with isolated PP.

Conventional computed tomography (CT) and high resolution CT (HRCT) have proved to be much more sensitive and specific than chest radiographs for the detection of pleural fibrosis [Aberle et al., 1988; Friedman et al., 1988; Gevenois et al., 1994], but in many countries chest radiographs remain the leading and often the only diagnostic tool for asbestos-related diseases. Over the last 20 years, the criteria used to distinguish PP from DPT in epidemiological studies have been very heterogeneous and often imprecise. The ILO classification of radiographs of pneumoconiosis, in the 1980 version [International Labour Office, 1980] has contributed to this fact as underlined by several authors [Bourbeau and Ernst, 1988; Parker et al., 1989; Hillerdal, 1991; Schwartz, 1991; Attfield and Wagner, 1992; Hilt et al., 1992]. In many publications, PP and DPT are not distinguished or diagnostic criteria are not described [Ohlson et al., 1985; Oliver et al., 1985, 1988; Hilt, 1987; Anton-Culver et al., 1989; Delclos et al., 1990; Balmes et al., 1991; Levin and Selikoff, 1991; Selikoff et al., 1991; Anderson et al., 1992; Ehrlich et al., 1992; Oksa et al., 1992; Welch et al., 1994]. Some authors quote the ILO classification, without any other details [Cotes and King, 1988; Hessel et al., 1988; Demers et al., 1990; Kilburn and Warshaw, 1990; Kouris et al., 1991; Bresnitz et al., 1993; Fischbein et al., 1993; Rey et al., 1993]. In order to facilitate the reading of pleural abnormalities and to reduce inter- and intra-reader variability, obliteration of costophrenic angle has been proposed to characterize DPT on postero-anterior chest-X-rays [Sargent et al., 1978; Bourbeau and Ernst, 1988; Bourbeau et al., 1990; Kennedy et al., 1991; Lilis et al., 1991, 1992; Miller et al., 1992; Schwartz et al., 1994; Garcia-Closas and Christiani, 1995]. Dimensional criteria have been proposed as an alternative definition for DPT [McLoud et al., 1985; De Klerk et al., 1989; AL Jarad et al., 1991; Yates et al., 1996].

The aim of the present multicenter retrospective study was to assess the relevance of this alternative definition compared to the definition based on obliteration of the costophrenic angle.

## MATERIALS AND METHODS

### Study Population

The study population consisted of 365 consecutive subjects, referred to occupational medicine departments in the Paris area (three centers) and in Normandy (two centers) for suspected asbestos-related pleural fibrosis, between 1992 and 1994.

Information on age, sex, tobacco consumption, height, weight, respiratory symptoms, chest pain, and asbestos

exposure (jobs, duration of exposure, time elapsed since the beginning of exposure), was obtained from case records. Additional information on cumulative exposure to asbestos was obtained for patients referred to Normandy centers. These patients were mainly former workers of a single asbestos textile and friction material factory. The subjects' occupational exposure was analyzed in collaboration with the company's medical department. The duration of occupational exposure to asbestos and the start and end dates of exposure were known for each subject. An intensity of exposure was defined for each job position based on dust measurements performed in numerous points of the workshops.

A cumulative exposure index, expressed in fibers/ml  $\times$  years was therefore calculated for each subject by determining the sum of the products [exposure  $\times$  duration] characterizing each job position, as previously described [Paris et al., 2002].

### Pulmonary Function Tests

The pulmonary function tests consisted of standard spirometry adhering to the American Thoracic Society Guidelines [American Thoracic Society, 1987].

Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV<sub>1</sub>), and total lung capacity (TLC) were expressed as percent predicted.

### Chest Radiographs

Postero-anterior chest radiographs, taken at maximum inspiration, were read independently by three among four experienced readers (JA, PB, ML, CR). For pleural abnormalities, site (chest wall, diaphragm, costophrenic angle), width, and extent were recorded separately, according to the ILO classification [International Labour Office, 2002].

### HRCT

In all subjects, HRCT was performed, mostly in the supine position, including at least five thin sections through the mid and lower thorax.

HRCT was considered to be the gold standard for the diagnosis of pleural thickening and pulmonary fibrosis.

The aims of HRCT were:

- a) to confirm the presence of pleural thickening;
- b) to detect parenchymal abnormalities suggestive of asbestosis.

HRCT were interpreted, independently of the chest X-rays, by consensus between the same readers as those examining the chest X-rays. They were considered to be consistent with asbestosis if at least one of the following abnormalities was present: bilateral septal or non-septal lines, subpleural curvilinear lines, or honeycombing.

## Analysis

Two radiographic definitions (definition 1, definition 2) were successively used to classify subjects into two groups: DPT group and PP group.

- *Definition 1*: DPT is characterized by pleural thickening of the chest wall, regardless of its width and extent, when associated and in continuity with an obliterated costophrenic angle.
- *Definition 2*: DPT is characterized by pleural thickening at least 5 mm wide and extending for more than one quarter of the chest wall (b2, b3, C2, C3, in the ILO classification), with or without obliteration of the costophrenic angle, as proposed by Yates et al. [1996].

Regardless of the definition used, pleural thickening not satisfying the diagnostic criteria of DPT was considered to be PP. When using definition 1, subjects were classified in the DPT group when at least two out of three readers recorded obliteration of the homolateral costophrenic angle. When using definition 2, subjects were classified in the DPT group when at least 2 out of 3 readers recorded pleural thickening  $\geq$  b2. In all cases, subjects in whom posteroanterior chest radiographs showed DPT and PP were classified in the DPT group.

Interreader agreement was evaluated successively with definitions 1 and 2. Sex, age, body mass index (BMI), tobacco consumption, characteristics of exposure (duration, latency period, cumulative exposure), respiratory symptoms, chest pain, and pulmonary function tests, were compared between the various DPT and PP groups, using the chi-square test or Student's *t* test. Multivariate analysis was performed to take into account potential confounding factors. Adjustments for gender, age, and tobacco consumption were made for respiratory symptoms, using logistic regression models. Adjustments for BMI and tobacco consumption were made for lung function tests, using multiple linear regression models. SAS software was used for calculations.

## RESULTS

Among the 365 subjects enrolled in the study, 73 were excluded from the analysis because of the absence of objective pleural thickening on HRCT ( $n=55$ ) or insufficient quality of the postero-anterior chest radiograph (quality 4 in the ILO classification for at least two readers,  $n=18$ ).

The remaining 287 subjects were mostly men (88%) with a mean age of 58 years; 68% were smokers or ex-smokers (Table I). In a large majority of subjects, occupational exposure to asbestos resulted from jobs involving the manufacture of asbestos-containing products (manufacture of asbestos-containing products: 69.7%, job in shipyards: 6.2%, insulation: 5.0%, welding: 4.1%; other: 15.0%). The mean duration of exposure to asbestos and time elapsed since

**TABLE I.** Demographic and Asbestos Exposure Characteristics of the Study Population (France)

	Population n = 287
Age (years): mean $\pm$ SD	58.0 $\pm$ 9.1
Sex	
Male	88.2%
Female	11.8%
Tobacco consumption	
Non-smokers	33.9%
Smokers	20.3%
Ex-smokers	45.8%
Asbestos exposure	
Duration (years): mean $\pm$ SD	25.4 $\pm$ 9.4
< 10 years	5.6%
10–19 years	18.9%
$\geq$ 20 years	75.5%
Latency (years): mean $\pm$ SD	33.5 $\pm$ 9.4
$\leq$ 30 years	35.8%
30–39 years	41.4%
$\geq$ 40 years	22.8%

the beginning of exposure (latency period) were 25 and 33 years respectively. For the 152 subjects from Normandy centers, mean cumulative exposure to asbestos was estimated at 255 f/ml.yrs.

When using definition 1, 11.8% of the study population were classified in the DPT group and 88.2% in the PP group. Complete agreement between readers (3 out of 3) concerning the presence or absence of obliteration of the costophrenic angle was obtained in 250 cases (87.1%) (Table II).

PP group and DPT group did not differ in terms of sex, age, tobacco consumption, duration of exposure to asbestos, and latency period (Table III). The mean cumulative exposure to asbestos was higher in the DPT group (323 vs. 249 f/ml.yrs), but the difference was not statistically significant (Table III). Chronic sputum, exertional dyspnea, and chest pain were significantly more prevalent in the DPT group than in the PP group (Table IV). The difference persisted after adjustment for age, sex, and tobacco consumption (data not shown). A marked decline in FVC,

**TABLE II.** Agreement Between Readers for Classification of the Study Population (France) in Pleural Plaques (PP) or Diffuse Pleural Thickening (DPT) Group When Using Definition 1 or 2

Agreement between readers	Definition 1	Definition 2	P
Full agreement (3/3)	250 (87.1%)	156 (54.4%)	a
Partial agreement (2/3)	37 (12.9%)	131 (45.6%)	

<sup>a</sup> $P < 0.001$ .

**TABLE III.** Demographic and Asbestos Exposure Characteristics of the Study Population (France), in PP and Diffuse Pleural Thickening (DPT) Groups According to Definition 1 and 2

	Definition 1			Definition 2		
	PP group n = 253	DPT group n = 34	P	PP group n = 185	DPT group n = 102	P
Sex: male	88.1%	88.2%	NS	84.9%	94.1%	<sup>b</sup>
Age (years): mean ± SD	57.8 ± 9.1	59.5 ± 9.8	NS	57.5 ± 8.6	58.9 ± 10.0	NS
BMI <sup>a</sup> : mean ± SD	26.8 ± 3.7	25.5 ± 3.5	<sup>b</sup>	26.4 ± 3.5	27.3 ± 4.0	<sup>b</sup>
Tobacco consumption						
Non-smokers	33.7%	35.3%		39.1%	24.5%	
Smokers	20.2%	20.6%	NS	20.1%	20.6%	<sup>b</sup>
Ex-smokers	46.1%	44.1%		40.8%	54.9%	
Duration of exposure (years): mean ± SD	25.4 ± 9.3	25.3 ± 10.2	NS	26.0 ± 9.1	24.3 ± 9.7	NS
< 10 years	5.2%	8.8%		3.8%	8.9%	
10–19 years	18.3%	23.5%	NS	19.0%	18.8%	NS
≥ 20 years	76.5%	67.7%		77.2%	72.3%	
Latency (years): mean ± SD	33.2 ± 9.2	35.6 ± 10.8	NS	33.2 ± 8.8	33.9 ± 10.4	NS
< 30 years	35.9%	35.2%		34.8%	37.6%	
30–39 years	42.6%	32.4%		44.0%	36.6%	NS
≥ 40 years	21.5%	32.4%	NS	21.2%	25.8%	
Cumulative exposure (f/mlyears): mean ± SD	249 ± 164 (n = 139)	323 ± 174 (n = 13)	NS	259 ± 168 (n = 110)	247 ± 161 (n = 42)	NS

<sup>a</sup>Body mass index:  $\frac{\text{weight (kg)}}{\text{height (m)}^2}$ .

<sup>b</sup>P < 0.05.

FEV<sub>1</sub>, and TLC was observed in subjects with DPT compared to subjects with PP. The differences persisted after adjustment for tobacco consumption and BMI.

As an unequal distribution of asbestosis in the groups could be partially responsible for the observed differences, similar comparisons were performed after exclusion of all subjects (n = 59) in whom HRCT showed parenchymal

abnormalities suggestive of asbestosis (Tables V, VI). A significant excess of chest pain and a significant decrease of FVC, FEV<sub>1</sub>, and TLC persisted in the DPT group compared to the PP group, even after adjustment for confounding factors.

When using definition 2 (dimensional criteria), 35.5% of the study population were classified in the DPT group and

**TABLE IV.** Respiratory Symptoms, Chest Pain, and Pulmonary Function Tests of the Study Population (France), in PP and Diffuse Pleural Thickening (DPT) Groups According to Definitions 1 and 2

	Definition 1			Definition 2		
	PP group n = 253	DPT group n = 34	P	PP group n = 185	DPT group n = 102	P
Chronic cough	33.5%	38.2%	NS	32.6%	36.6%	NS
Chronic sputum	18.8%	35.3%	<sup>a</sup>	17.9%	26.0%	NS
Chronic bronchitis	14.4%	21.2%	NS	14.8%	16.0%	NS
Exertional dyspnea	34.5%	54.6%	<sup>a</sup>	35.5%	43.8%	NS
Chest pain	18.5%	42.4%	<sup>b</sup>	19.3%	25.3%	NS
FVC (% predicted): mean ± SD	96.1 ± 15.4	81.1 ± 17.2	<sup>c</sup>	95.6 ± 16.4	91.3 ± 16.8	NS
FEV <sub>1</sub> (% predicted): mean ± SD	94.5 ± 18.2	75.5 ± 15.8	<sup>c</sup>	93.1 ± 19.8	90.7 ± 17.4	NS
TLC (% predicted): mean ± SD	92.2 ± 12.3	80.5 ± 16.6	<sup>c</sup>	91.8 ± 13.3	88.8 ± 13.4	NS

<sup>a</sup>P < 0.05.

<sup>b</sup>P < 0.01.

<sup>c</sup>P < 0.001.

**TABLE V.** Demographic and Exposure Characteristics of the Study Population (France), in PP and Diffuse Pleural Thickening (DPT) Groups According to Definitions 1 and 2, After Exclusion of Subjects With Parenchymal Abnormalities Suggestive of Asbestosis on HRCT

	Definition 1			Definition 2		
	PP group n = 205	DPT group n = 23	P	PP group n = 153	DPT group n = 75	P
Sex: men	86.8%	82.6%	NS	83.7%	92.0%	NS
Age (years): mean $\pm$ SD	57.3 $\pm$ 9.0	58.9 $\pm$ 10.2	NS	57.0 $\pm$ 8.6	58.3 $\pm$ 10.3	NS
BMI <sup>a</sup> : mean $\pm$ SD	26.9 $\pm$ 3.7	26.0 $\pm$ 3.9	NS	26.5 $\pm$ 3.5	27.5 $\pm$ 4.1	NS
Tobacco consumption						
Non-smokers	37.8%	43.5%		42.1%	30.7%	
Smokers	19.1%	13.0%	NS	19.1%	17.4%	NS
Ex-smokers	43.1%	43.5%		38.8%	52.0%	
Duration of exposure (years): mean $\pm$ SD	25.6 $\pm$ 9.5	28.1 $\pm$ 8.8	NS	26.3 $\pm$ 9.2	24.9 $\pm$ 9.8	NS
< 10 years	4.9%	0.0%		3.3%	6.7%	
10–19 years	17.7%	21.7%	NS	18.4%	17.3%	NS
$\geq$ 20 years	77.5%	78.3%		78.3%	76.0%	
Latency (years): mean $\pm$ SD	33.0 $\pm$ 9.4	34.9 $\pm$ 10.3	NS	33.2 $\pm$ 9.2	33.3 $\pm$ 10.0	NS
< 30 years	36.8%	30.4%		35.5%	37.3%	
30–39 years	40.7%	43.5%	NS	41.5%	40.0%	NS
$\geq$ 40 years	22.6%	26.1%		23.0%	22.7%	
Cumulative exposure (f/ml.years): mean $\pm$ SD	236 $\pm$ 161 (n = 114)	323 $\pm$ 174 (n = 13) <sup>2</sup>	0.07	245 $\pm$ 165 (n = 93)	243 $\pm$ 163 (n = 34)	

<sup>a</sup>Body mass index:  $\frac{\text{weight (kg)}}{\text{height (m)}^2}$ .

64.5% in the PP group. Complete agreement between readers concerning the presence or absence of pleural thickening  $\geq$  b2 was obtained in 156 cases (54.4%) (Table II). The PP group and the DPT group differed slightly with respect to sex ratio, BMI, and tobacco consumption (more men, higher BMI, more smokers, and ex-smokers in the DPT group) (Table III). They did not differ concerning the characteristics of asbestos exposure. Respiratory symptoms and chest pain

were slightly more prevalent in the DPT group than in the PP group and impairment of pulmonary function tests were slightly more pronounced in the DPT group, but the differences were not statistically significant (Table IV).

The same comparisons, performed after exclusion of subjects in whom HRCT showed parenchymal abnormalities suggestive of asbestosis, did not show any significant difference between the two groups (Tables V, VI).

**TABLE VI.** Respiratory Symptoms, Chest Pain, and Pulmonary Function Tests of the Study Population (France), in PP and Diffuse Pleural Thickening (DPT) Groups According to Definitions 1 and 2, After Exclusion of Subjects With Parenchymal Abnormalities Suggestive of Asbestosis on HRCT

	Definition 1			Definition 2		
	PP group n = 205	DPT group n = 23	P	PP group n = 153	DPT group n = 75	P
Chronic cough	31.0%	30.4%	NS	30.3%	32.4%	NS
Chronic sputum	18.8%	26.1%	NS	17.1%	24.7%	NS
Chronic bronchitis	14.8%	8.7%	NS	14.5%	13.5%	NS
Exertional dyspnea	33.3%	47.8%	NS	32.7%	39.2%	NS
Chest pain	19.2%	45.5%	<sup>a</sup>	20.8%	23.9%	NS
FVC (% predicted): mean $\pm$ SD	96.1 $\pm$ 15.5	83.8 $\pm$ 18.6	<sup>a</sup>	95.7 $\pm$ 16.8	92.2 $\pm$ 15.0	NS
FEV <sub>1</sub> (% predicted): mean $\pm$ SD	94.6 $\pm$ 18.5	75.9 $\pm$ 17.4	<sup>b</sup>	93.2 $\pm$ 20.1	91.9 $\pm$ 17.2	NS
TLC (% predicted): mean $\pm$ SD	92.6 $\pm$ 12.4	80.9 $\pm$ 15.2	<sup>b</sup>	91.9 $\pm$ 13.6	90.5 $\pm$ 12.2	NS

<sup>a</sup>P < 0.01.

<sup>b</sup>P < 0.001.



**TABLE VII.** Concordance Between Classification of the Study Population (France), in PP Group or Diffuse Pleural Thickening (DPT) Group With the Two Definitions

	Definition 1		Total
	PP	DPT	
Definition 2			
PP	170	15	185
DPT	83	19	102
Total	253	34	287

Overall, 189 subjects (65.8%) were classified in the same groups according to the two definitions. 83 of the 102 subjects (81.3%) considered to have DPT according to definition 2 were considered to have PP according to definition 1 (Table VII).

## DISCUSSION

In the near future, computed tomography will probably become the investigation of choice for the surveillance of workers with present or past exposure to asbestos in most wealthy industrialized countries. However the majority of asbestos-exposed workers live in developing countries where chest radiography remains and will probably remain for a long time the only diagnostic tool for asbestos-related diseases. It has been demonstrated that DPT and PP are associated with different levels of impairment of lung function [Schwartz, 1991; Rudd, 1996; Ameille and Letourneux, 1998; Chailleux and Letourneux, 1999]. They also have different dose determinants [Gibbs et al., 1991] and therefore different prognostic implications. Consequently, it is still useful to define accurate criteria to distinguish diffuse and circumscribed pleural thickening by radiography.

In our study population, the distinction between PP and DPT, based on dimensional criteria regardless of the appearance of the costophrenic angle, did not reveal any significant differences between the two groups, either in terms of frequency of respiratory symptoms, or degree of respiratory impairment, or the characteristics of asbestos exposure. On the other hand, the distinction between DPT and PP based on obliteration of costophrenic angle, enabled us to characterize two different populations.

Subjects with DPT were less numerous than subjects with PP. They more frequently presented respiratory symptoms—chronic sputum, exertional dyspnea, and chest pain—than subjects with PP. They presented a higher level of impairment of lung function. Furthermore, these differences persisted after adjustment for potential confounding variables and after exclusion of subjects with parenchymal abnormalities suggestive of asbestosis. The mean cumulative

exposure to asbestos was also higher, although not significantly, in subjects with DPT.

These results are consistent with those of previous studies. The small number of cases of DPT observed in the study, compared to the number of PP, is in agreement with studies using a similar radiological characterization of DPT [Bourbeau et al., 1990; Schwartz et al., 1990; Lilis et al., 1991, 1992; Miller et al., 1992; Fischbein et al., 1993; Garcia-Closas and Christiani, 1995].

The association between obliteration of the costophrenic angle and a significant decrease of FVC, FEV<sub>1</sub>, and TLC, has also been observed previously. In a cohort of 1,211 sheet metal workers, the decrease of FVC was twofold greater in subjects with DPT characterized by obliteration of the costophrenic angle, than in subjects with PP [Schwartz et al., 1990]. In a cohort of 1,985 insulation workers with pleural thickening, obliteration of the costophrenic angle, even with limited pleural fibrosis, resulted in a marked reduction of FVC [Lilis et al., 1991]. In a cross-sectional study of 110 construction workers, an analysis of the independent effects of pleural changes, at different sites, on respiratory function, showed that most marked impairment of the lung function was related to costophrenic angle obliteration [Bourbeau et al., 1990].

Furthermore, the agreement between readers concerning the presence or absence of costophrenic angle obliteration was significantly better than the agreement concerning the width and extent of pleural thickening, corroborating a previous report from Bourbeau and Ernst [1988].

Some authors consider that DPT might result either from fibrosis of visceral pleura or from confluent plaques [McLoud et al., 1985; Staples et al., 1992]. However, there is now a large consensus that DPT is the radiographic expression of thickening and fibrosis of the visceral pleura, often associated with fusion of the parietal pleura, following clearance of benign asbestos-related pleural effusion [Hillerdal et al., 1990; Schwartz, 1991; Solomon, 1991; Miller et al., 1993; Rudd, 1996; Consensus Report, 1997; Gevenois et al., 1998; Chailleux and Letourneux, 1999; Peacock et al., 2000]. Several studies have confirmed that DPT is preceded by a benign asbestos pleural effusion [Martensson et al., 1987; Miller and Miller, 1993]. Obliteration of the costophrenic angle represents the sequela of pleural effusion. It therefore appears logical to propose this criterion for the diagnosis of DPT.

Nevertheless, some authors consider that the radiographic diagnosis of DPT based on obliteration of the costophrenic angle might underdiagnose this entity [Kee et al., 1996]. Indeed the use of CT or HRCT has shown that fibrosis of visceral pleura, as attested by the presence of parenchymal bands and/or rounded atelectasis, may occur without obliteration of the costophrenic angle [Bayeux et al., 1998; Gevenois et al., 1998]. However, dimensional criteria are a source of confusion. They cannot reliably distinguish

between fibrosis of visceral and parietal pleural, or even between pleural fibrosis and subpleural fat pads. This explains the high proportion of DPT among subjects with pleural thickening in studies in which the definition of DPT is based on dimensional criteria. In our study, using the criteria proposed by Yates et al. [1996], DPT represented 36% of all pleural thickenings. Similarly, in a cohort of 1,373 asbestos-exposed workers, the number of DPT, defined as smooth uninterrupted pleural densities extending over at least one quarter of the chest wall, was nearly the same as the number of PP [McLoud et al., 1985].

In conclusion, if we accept that the term DPT should only be used when fibrosis of the visceral pleura is suspected, then obliteration of the costophrenic angle on postero-anterior chest X-ray appears to be a much more reliable sign than dimensional criteria. Fortunately, the ILO 2000 classification of radiographs of pneumoconiosis [International Labour Office, 2002] has retained this criterion for the diagnosis of DPT. Recording of the presence of parenchymal bands and/or rounded atelectasis, which are now considered to be radiological signs of involvement of the visceral pleura [Hillerdal et al., 1990; Consensus Report, 1997; Bayeux et al., 1998; Gevenois et al., 1998], may improve the sensitivity of postero-anterior chest X-ray for the diagnosis of DPT. Furthermore, our results confirm that it is very important to distinguish DPT from PP, from a medical as well as a forensic point of view, as DPT is associated with a high prevalence of chest pain and significant lung function impairment.

## REFERENCES

- Aberle DR, Gamsu G, Ray CS. 1988. High-resolution CT of benign asbestos-related diseases: Clinical and radiographic correlation. *AJR* 151:883–891.
- Al Jarad N, Poulakis N, Pearson M, Rubens MP, Rudd RM. 1991. Assessment of asbestos-induced pleural disease by computed tomography. Correlation with chest radiography and lung function. *Respir Med* 85:203–208.
- Ameille J, Letourneux M. 1998. Les pathologies asbestosiques non tumorales. *Rev Mal Respir* 15:479–487.
- American Thoracic Society. 1987. Standardization of spirometry. 1987 update. *Am Rev Respir Dis* 136:1285–1298.
- Anderson HA, Hanrahan LP, Higgins DN, Sarow PG. 1992. A radiographic survey of public school building maintenance and custodial employees. *Environ Res* 59:159–166.
- Anton-Culver H, Culver BD, Kurosaki T. 1989. An epidemiologic study of asbestos-related chest X-ray changes to identify work areas of high risk in a shipyard population. *Appl Ind Hyg* 4:110–118.
- Attfield MD, Wagner GR. 1992. A report on a workshop of the National Institute for Occupational Safety and health B reader certification program. *J Occup Med* 34:875–878.
- Balmes JR, Daponte A, Cone JE. 1991. Asbestos-related disease in custodial and building maintenance workers from a large municipal school district. *Ann NY Acad Sci* 643:540–549.
- Bayeux MC, Letourneux M, Brochard P, Raffaelli C, Pairon JC, Iwatsubo Y, Ameille J. 1998. Atelectasie par enroulement et amiante. A propos de 26 cas. *Rev Mal Respir* 15:281–286.
- Bourbeau J, Ernst P. 1988. Between and within reader variability in the assessment of asbestos-related pleural disease using the ILO 1980 international classification of pneumoconiosis. *Am J Ind Med* 14:537–543.
- Bourbeau J, Ernst P, Chrome J, Armstrong B, Becklake M. 1990. The relationship between respiratory impairment and asbestos-related pleural abnormality in an active work force. *Am Rev Respir Dis* 142:837–842.
- Bresnitz EA, Gilman MJ, Gracely EJ, Avioldi J, Vogel E, Geftter W. 1993. Asbestos-related radiographic abnormalities in elevator construction workers. *Am Rev Respir Dis* 147:1341–1344.
- Chailleux E, Letourneux M. 1999. Impact médical du dépistage des lésions pleurales bénignes liées à l'inhalation de poussières d'amiante. *Rev Mal Respir* 16:1286–1293.
- Consensus Report—Asbestos, Asbestosis, and Cancer. 1997. The Helsinki criteria for diagnosis and attribution. *Scand J Work Environ Health* 23:311–316.
- Cotes JE, King B. 1988. Relationship of lung function to radiographic reading (ILO) in patients with asbestos-related lung disease. *Thorax* 43:777–783.
- de Klerk NH, Cookson WO, Armstrong BK, Glancy JL. 1989. Natural history of pleural thickening after exposure to crocidolite. *Br J Ind Med* 46:461–467.
- Delclos GL, Wilson K, Bradley BL. 1990. Influence of smoking on radiographic profusion and pleural changes in asbestos-exposed subjects. *J Occup Med* 131:499–504.
- Demers RY, Neale AV, Robins T, Hermans SC. 1990. Asbestos-related pulmonary disease in boilermakers. *Am J Ind Med* 17:327–339.
- Ehrlich R, Lilis R, Chan E, Nicholson W, Selikoff IJ. 1992. Long term radiological effects of short term exposure to amosite asbestos among factory workers. *Br J Ind Med* 49:268–275.
- Fischbein A, Luo JCJ, Lacher M, Rosenfeld S, Rosenbaum A, Miller A, Solomon SJ. 1993. Respiratory findings among millwright and machinery erectors: Identification of health hazards from asbestos in place at work. *Environ Res* 61:25–35.
- Friedman AC, Fiel SB, Fisher MS, Radecke PD, Lev-Toaff AS, Caroline DT. 1988. Asbestos-related pleural disease and asbestosis a comparison of CT and chest radiography. *AJR* 150:269–275.
- Garcia-Closas M, Christiani DC. 1995. Asbestos-related diseases in construction carpenters. *Am J Ind Med* 27:115–125.
- Gevenois PA, De Vuyst P, Dedeire S, Cosaerts J, Vande Weyer R, Struyven J. 1994. Conventional and high-resolution CT in asymptomatic asbestos-exposed workers. *Acta Radiol* 35:226–229.
- Gevenois PA, Martelaer V, Madani A, Sergeant G, De Vuyst P. 1998. Asbestos, pleural plaques, and diffuse pleural thickening: Three distinct benign responses to asbestos exposure. *Eur Respir J* 11:1021–1027.
- Gibbs AR, Stephens M, Griffith DM, Blight BJN, Pooley F. 1991. Fibre distribution in the lungs and pleura of subjects with asbestos-related diffuse pleural fibrosis. *Br J Ind Med* 48:762–770.
- Hessel PA, Melenka LS, Michaelchuk F, Herbert FA, Cowie RL. 1988. Lung health among plumbers and pipefitters in Edmonton, Alberta. *Occup Environ Health* 55:678–683.
- Hillerdal G. 1991. Pleural lesions and the ILO classification: The need for a revision. *Am J Ind Med* 19:125–130.
- Hillerdal G, Malmberg P, Hemmingson A. 1990. Asbestos-related lesions of the pleura: Parietal plaques compared to diffuse thickening



- studied with chest roentgenography, computed tomography, lung function, and gas exchange. *Am J Ind Med* 18:627–639.
- Hilt B. 1987. Non malignant asbestos diseases in workers in an electrochemical plant. *Br J Ind Med* 44:621–626.
- Hilt B, Borgersen A, Lien JT, Langard S. 1992. Chest radiographs in subjects with asbestos-related abnormalities: Comparison between ILO categorizations and clinical reading. *Am J Ind Med* 21:855–861.
- International Labour Office. 1980. Guidelines for the use of the ILO classification of radiographs of pneumoconioses. Occupational Health and Safety Series, no. 22. Geneva.
- International Labour Office. 2002. Guidelines for the use of the ILO international classification of radiographs of pneumoconiosis. Occupational safety and health series, no. 22, Geneva.
- Kee ST, Gamsu G, Blanc P. 1996. Causes of pulmonary impairment in asbestos-exposed individuals with diffuse pleural thickening. *Am J Respir Crit Med* 154:789–793.
- Kennedy SM, Vedal S, Müller N, Kassam A, Chan-Yeung M. 1991. Lung function and chest radiograph abnormalities among construction insulators. *Am J Ind Med* 20:673–684.
- Kilburn KH, Warshaw R. 1990. Pulmonary functional impairment associated with pleural asbestos disease. Circumscribed and diffuse thickening. *Chest* 98:965–972.
- Kouris SP, Parker DL, Bender AP, Williams AN. 1991. Effects of asbestos-related pleural disease on pulmonary function. *Scand J Work Environ Health* 17:179–183.
- Levin SM, Selikoff IJ. 1991. Radiological abnormalities and asbestos exposure among custodians of the New-York city board of education. *Ann NY Acad Sci* 643:530–539.
- Lilis R, Miller A, Godbold J, Chan E, Selikoff IJ. 1991. Pulmonary function and pleural fibrosis: Quantitative relationship with an integrative index of pleural abnormalities. *Am J Ind Med* 20:145–161.
- Lilis R, Miller A, Godbold J, Benkert S, Wu V, Selikoff IJ. 1992. Comparative quantitative evaluation of pleural fibrosis and its effects on pulmonary function in two large asbestos-exposed occupational groups—insulators and sheet metal workers. *Environ Res* 59:49–66.
- Lynch DA, Gamsu D, Aberle DR. 1989. Conventional and high resolution computed tomography in the diagnosis of asbestos-related diseases. *Radiographics* 9:523–581.
- Martensson G, Habberg S, Pettersson K, Thiringer G. 1987. Asbestos pleural effusion: A clinical entity. *Thorax* 42:646–651.
- McCloud TC, Woads BO, Carrington CB, Epler GR, Gaensler EA. 1985. Diffuse pleural thickening in an asbestos-exposed population: Prevalence and causes. *AJR* 144:9–18.
- Miller A, Miller JA. 1993. Diffuse thickening superimposed on circumscribed pleural thickening related to asbestos exposure. *Am J Ind Med* 23:859–871.
- Miller A, Lilis R, Godbold J, Chan E, Selikoff IJ. 1992. Relationship of pulmonary function to radiographic interstitial fibrosis in 2611 long-term asbestos insulators. *Am Rev Respir Dis* 145:263–270.
- Ohlson CG, Bodin L, Rydman T, Hogstedt C. 1985. Ventilatory decrements in former asbestos cement workers: A four year follow up. *Br J Ind Med* 42:612–616.
- Oksa P, Koskinen H, Rinne JP, Zitting A, Proto P, Huuskonen MS. 1992. Parenchymal and pleural fibrosis in construction workers. *Am J Ind Med* 21:561–567.
- Oliver LC, Eisen EA, Greene RE, Sprince NL. 1985. Asbestos-related disease in railroad workers. A cross-sectional study. *Am Rev Respir Dis* 131:499–504.
- Oliver LC, Eisen EA, Greene R, Sprince NL. 1988. Asbestos-related pleural plaques and lung function. *Am J Ind Med* 14:649–656.
- Paris C, Galateau-Salle F, Chevreuil C, Morella R, Raffaelli C, Gillon JC, Billon-Galland MA, Paire JC, Chevreau L, Letourneux M. 2002. Asbestos bodies in the sputum of asbestos workers: Correlation with asbestos exposure. *Eur Respir J* 20:1167–1173.
- Parker DL, Bender AP, Hankinson S, Aeppel D. 1989. Public health implications of the variability in the interpretation of “B” readings for pleural changes. *J Occup Med* 31:775–780.
- Peacock C, Copley SJ, Hanselle DM. 2000. Asbestos-related benign pleural disease. *Clin Radiol* 55:422–432.
- Rey F, Boutin C, Steinbauer J, Viallat JR, Alessandrini P, Jutisz P, Di Giambattista D, Billon-Galland MA, Hereng P, Dumortier P, De Vuyst P. 1993. Environmental pleural plaques in an asbestos exposed population of northeast Corsica. *Eur Respir J* 6:978–982.
- Rudd RM. 1996. New developments in asbestos-related pleural disease. *Thorax* 51:210–216.
- Sargent EN, Gordanson JS, Jacobson G, Birnbaum W, Shaut B. 1978. Bilateral pleural thickening. A manifestation of asbestos dust exposures. *AJR* 131:579–585.
- Schwartz DA. 1991. New developments of asbestos-induced pleural disease. *Chest* 99:191–198.
- Schwartz DA, Fuertes JJ, Galvin JR, Burmeister LF, Schmidt LE, Lustikow BN, Lamarte FP, Merchant JA. 1990. Asbestos-induced pleural fibrosis and impaired lung function. *Am Rev Respir Dis* 141:321–326.
- Schwartz DA, Davis CS, Merchant JA, Bunn WB, Galvin JR, Van Fossen DS, Dayton CS, Hunninghake GW. 1994. Longitudinal changes in lung function among asbestos-exposed workers. *Am J Respir Crit Care Med* 150:1243–1249.
- Selikoff IJ, Lilis R. 1991. Radiological abnormalities among sheet-metal workers in the construction industry in the United-States and Canada—relationship to asbestos-exposure. *Arch Environ Health* 46:30–36.
- Solomon A. 1991. Radiological features of asbestos-related visceral pleural changes. *Am J Ind Med* 19:339–355.
- Staples CA. 1992. Computed tomography in the evaluation of benign asbestos-related disorders. *Radiol Clin N Am* 30:1191–1207.
- Welch LS, Michaels D, Zoloth SR, the National Sheet Metal Examination Group. 1994. The national sheet metal workers asbestos disease screening program: Radiological findings. *Am J Ind Med* 25:635–648.
- Yates D, Browne K, Stidolph PN, Neville E. 1996. Asbestos-related bilateral diffuse pleural thickening: Natural history of radiographic and lung function abnormalities. *Am J Respir Crit Care Med* 153:301–306.